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COMMENTARY
Long-term cognitive effects of drugs used during labor

Kristine Yaffe

Department of Psychiatry and Neurology, University of California, San Francisco, 4150 Clement Street, San Francisco, CA 94121

Sumner J Yaffe

Center for Research on Mothers and Children, National Institute of Child Health and Human Development, National Institutes of Health, Building 61, Bethesda, MD 20892

Oxytocin, a hormone produced by the posterior pituitary gland, stimulates uterine smooth muscle during labor, contracts uterine vessels, and induces milk letdown. It is available as a synthetic compound and is used to induce uterine contraction during labor in 15-40% of parturients and to diminish blood loss in almost all women during the final stage of labor.[1] High doses of oxytocin may result in hyperstimulation of the uterus and may pose an appreciable risk to the mother and fetus; risks to the fetus include hypoxia and damage to the central nervous system.[2] The long-term consequences for the infant of oxytocin and other commonly used drugs have not been well studied. In particular, the behavioral and cognitive outcomes of pharmacological treatments used during labor have received little attention. This has partially been due to the tremendous expense of and difficulty in following cohorts of infants and studying them over decades.[3] The challenge of adjusting for potential confounders (such as socioeconomic, nutritional and educational status) from the time of exposure in utero through to adulthood are also enormous.

Sorensen et al have met some of these challenges with their study of a cohort of 4300 draft-age men from two Danish counties who completed a Danish intelligence test, the Boerge Prien test, as part of the screening examination for the draft.[4] The draftees were linked to the Danish medical birth registry, a database containing data on all births since 1973. Altogether, 1011 (22.8%) of the men had been exposed to oxytocin in utero; their mean intelligence score was not significantly different from those who were not exposed, even after multivariate adjustments. This rare opportunity to follow a cohort from birth to adulthood with complete ascertainment is laudable. Further strengths of the study are its large sample size and its community-based population.

More information on the dose of oxytocin and, most importantly, at which stage of labor it was administered would have provided more conclusive evidence. Exposure during the third stage of labor (postpartum) would not be expected to affect the newborn whereas exposure during earlier stages might have an effect on the central nervous system of the fetus.[5] In addition, a selection bias could explain the lack of an association since 495 men were exempted from the examination on medical grounds due to illnesses which included epilepsy. Although the percentage of those exposed to oxytocin was similar for the men who were examined and those who were not, it would have been useful to determine if those with epilepsy had had a similar exposure rate. Epilepsy is often an indication of widespread central nervous system injury[6] that, in turn, may be associated with poor cognitive function. It would also have been useful to determine the educational performance of the cohort to see if functional differences existed between the exposed and unexposed groups. It is also possible that gender differences exist; Seidman et al found that neonatal hyperbilirubinemia was associated with lower scores on intelligence tests in male 17-year-olds but not in females.[7] Interestingly, they did not find a significant association between IQ score and hyperbilirubinemia when it was analyzed as a continuous variable but did when IQ was dichotomized to a low score. It would be interesting to explore whether Sorensen et al stratified the groups by performance and if there was an association between poor performance and exposure to oxytocin.

Long-term consequences, especially cognitive and behavioral, of drugs administered during labor and delivery have not been studied often. The findings by Sorensen et al are a significant contribution towards answering an important question. More research on the effects of drug exposure in utero should be pursued.

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